

### REMARKS

Claims 1-12 and 20-25 are pending. Applicants have canceled claim 12, amended claims 1, 9 and 11, and added claim 26 herewith. Support for the amendments appears throughout the specification and claims as originally filed, including at page 7, lines 13-15 and pages 8-13 and page 18 of the specification. No new matter is introduced by these amendments. Applicants make these amendments in order to expedite prosecution of these claims. Applicants make such amendments without prejudice to pursuing the originally presented or cancelled subject matter in a later application claiming benefit of this application, and particularly without prejudice to determination of equivalents of subject matter of this application or any later application claiming benefit of this application.

#### Specification

Applicants have amended the title as suggested by the Examiner.

#### Rejection under 35 U.S.C. § 112, second paragraph

Claim 9 is rejected as indefinite for reciting the limitation "converting the resultant compound of formula (I) into a further compound of formula (I)". Applicants have amended claim 9 to remove this phrase. Applicants submit that amended claim 9 is not indefinite and request withdrawal of the rejection.

Claim 11 is rejected as an improper multiple-dependent claim. Applicants have amended claim 11 to depend from claim 1. Applicants submit that amended claim 11 is not a multiple-dependent claim and request withdrawal of the rejection.

#### Rejection under 35 U.S.C. § 102(b)

Claims 1 and 5-7 (which are dependent from claim 1) are rejected as anticipated by Zayed et al. (CA 101:54985), it being alleged that 3-[(aminomethylthioxomethyl)amino]-5-phenyl-1H-pyrazole-4-carboxamide (the "Zayed Compound") is embraced by formula (I) in claim 1. Applicants have amended claim 1 to recite a compound of formula (I) where the A

group is thiophene, furan, pyrrole, imidazole, thiazole or oxazole. As such, the Zayed Compound, which has a pyrazole as the group corresponding to the A group in Applicants' formula (I) compounds, does not anticipate Applicants' formula (I) compounds as recited in amended claim 1. Applicants therefore submit that claim 1, as amended, is not anticipated by Zayed et al. and request that this rejection be withdrawn.

Objections

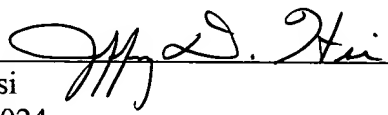
Claims 2, 3, 4, 8, 10, 12, and 20-25 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form. Applicants have canceled claim 12 herewith. Applicants note that claims 2, 3, 4, 8, 10 and 20-25 all depend from claim 1. As claim 1 is amended to be allowable, claims 2, 3, 4, 8, 10 and 20-25 are no longer dependent upon a rejected base claim. Applicants request that this objection be withdrawn.

Attached is a marked-up version of the changes being made by the current amendment.

Applicant respectfully asks that all claims be allowed. Please apply any other charges or credits to Deposit Account No. 06-1050, referencing attorney docket number 06275-233001.

Respectfully submitted,

Date: February 10, 2003

  
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**Version with markings to show changes made**

**In the specification:**

The title has been amended as follows:

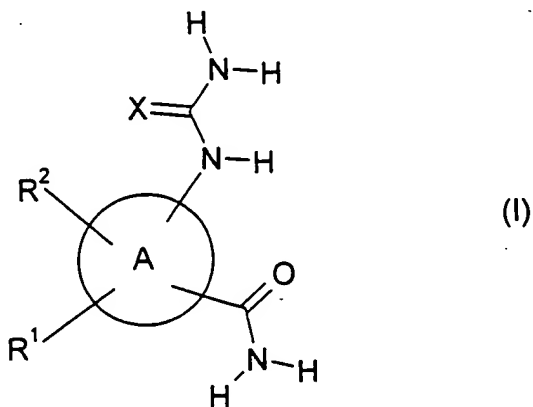
-- [NOVEL COMPOUNDS]UREA-CARBOXAMIDE-HETEROARYL COMPOUNDS  
AS INHIBITORS OF IKK2 --

**In the claims:**

Claim 12 has been cancelled.

Claims 1, 9 and 11 have been amended as follows:

-- 1 (Amended). A compound of formula (I)



in which:

A represents [a 5-membered heteroaromatic ring containing one or two heteroatoms selected independently from oxygen, nitrogen or sulfur] thiophene, furan, pyrrole, imidazole, thiazole or oxazole;

R<sup>1</sup> represents a phenyl group or a 5- to 7-membered heteroaromatic ring containing one to three heteroatoms selected independently from oxygen, nitrogen or sulfur; said phenyl or

heteroaromatic ring being optionally substituted by one or more substituents selected independently from halogen, cyano, nitro,  $-\text{NR}^3\text{R}^4$ ,  $-\text{CONR}^5\text{R}^6$ ,  $-\text{COOR}^7$ ,  $-\text{NR}^8\text{COR}^9$ ,  $-\text{SR}^{10}$ ,  $-\text{S(O)}_m\text{R}^{10}$ ,  $-\text{S(O)}_2\text{NR}^5\text{R}^6$ ,  $-\text{NR}^8\text{SO}_2\text{R}^{10}$ ,  $\text{C}_1\text{-C}_6$  alkyl, trifluoromethyl,  $-(\text{CH}_2)_n\text{R}^{11}$ ,  $-\text{O}(\text{CH}_2)_n\text{R}^{11}$  or  $-\text{OR}^{12}$ ;

$\text{R}^2$  represents hydrogen, halogen, cyano, nitro,  $-\text{NR}^{13}\text{R}^{14}$ ,  $-\text{CONR}^{15}\text{R}^{16}$ ,  $-\text{COOR}^{17}$ ,  $-\text{NR}^{18}\text{COR}^{19}$ ,  $-\text{S(O)}_m\text{R}^{20}$ ,  $-\text{S(O)}_2\text{NR}^{15}\text{R}^{16}$ ,  $-\text{NR}^{18}\text{SO}_2\text{R}^{20}$ ,  $\text{C}_1\text{-C}_2$  alkyl, trifluoromethyl,  $\text{C}_2\text{-C}_3$  alkenyl,  $\text{C}_2\text{-C}_3$  alkynyl, trifluoromethoxy,  $\text{C}_1\text{-C}_2$  alkoxy or  $\text{C}_1\text{-C}_2$  alkanoyl;

X represents oxygen or sulfur;

each of  $\text{R}^3$ ,  $\text{R}^4$ ,  $\text{R}^5$ ,  $\text{R}^6$ ,  $\text{R}^7$ ,  $\text{R}^8$ ,  $\text{R}^9$ ,  $\text{R}^{10}$  and  $\text{R}^{12}$  independently represent a hydrogen atom or  $\text{C}_1\text{-C}_6$  alkyl;

$\text{R}^{11}$  represents  $\text{NR}^{21}\text{R}^{22}$  where  $\text{R}^{21}$  and  $\text{R}^{22}$  are independently hydrogen or  $\text{C}_1\text{-C}_6$  alkyl optionally substituted by  $\text{C}_1\text{-C}_4$  alkoxy; or  $\text{R}^{21}$  and  $\text{R}^{22}$  together with the nitrogen atom to which they are attached form a 5- or 6-membered saturated ring optionally containing a further O, S or  $\text{NR}^{23}$  group where  $\text{R}^{23}$  is hydrogen or  $\text{C}_1\text{-C}_6$  alkyl; or  $\text{R}^{11}$  represents  $\text{OR}^{24}$  where  $\text{R}^{24}$  represents  $\text{C}_1\text{-C}_6$  alkyl;

each of  $\text{R}^{13}$ ,  $\text{R}^{14}$ ,  $\text{R}^{15}$ ,  $\text{R}^{16}$ ,  $\text{R}^{17}$ ,  $\text{R}^{18}$ ,  $\text{R}^{19}$  and  $\text{R}^{20}$  independently represent a hydrogen atom or  $\text{C}_1\text{-C}_2$  alkyl;

m represents an integer 0, 1 or 2;

n represents an integer 2, 3 or 4;

and optical isomers, racemates, and tautomers thereof and pharmaceutically acceptable salts or solvates thereof:

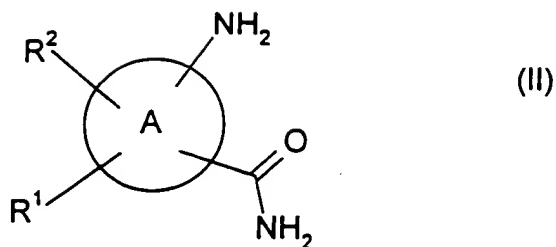
provided that:

when A represents thiophene, furan or pyrrole, then  $\text{R}^1$  is not 4-pyridinyl or 3-pyrazolyl; and

when A represents oxazole, thiazole or imidazole, then  $\text{R}^1$  is not 3-pyridinyl or 5-pyrimidyl.

9 (Twice Amended). A process for the preparation of a compound of formula (I), according to claim 1, which comprises:

(a) reaction of a compound of formula (II):

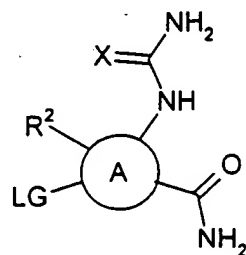


wherein A, R<sup>1</sup> and R<sup>2</sup> are as defined in Claim 1 with an isocyanate (X = O) or an isothiocyanate (X = S); or

(b) reaction of compound of formula (III) with a compound of formula (IV)

R<sup>1</sup>-Metal

(III)

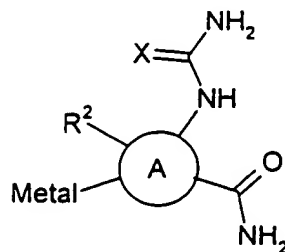


wherein A, X, R<sup>1</sup> and R<sup>2</sup> are as defined in Claim 1 and LG represents a leaving group; or

(c) reaction of compound of formula (V) with a compound of formula (VI)

R<sup>1</sup>-LG

(V)



wherein A, X, R<sup>1</sup> and R<sup>2</sup> are as defined in Claim 1 and LG represents a leaving group;

and where necessary converting the resultant compound of formula (I), or another salt thereof, into a pharmaceutically acceptable salt thereof; [or converting the resultant compound of formula (I) into a further compound of formula (I);] and where desired converting the resultant compound of formula (I) into an optical isomer thereof.

11 (Amended). A process for the preparation of a pharmaceutical composition [as claimed in Claim 10] which comprises mixing a compound of formula (I), or a pharmaceutically acceptable salt or solvate thereof, as claimed in [any one of claims] claim 1 [to 8] with a pharmaceutically acceptable adjuvant, diluent or carrier.--